Pseudoachalasia as a Result of Metastatic Cervical Cancer

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ABSTRACT

Background: Distinguishing achalasia from pseudoachalasia can be difficult, as the clinical, radiological, and manometric findings can be similar to those seen in achalasia.

The features that may differentiate achalasia from pseudoachalasia are reviewed and the pathogenesis of pseudoachalasia is discussed.

Methods: A patient presented with a clinical scenario of achalasia that was documented by radiographic, endoscopic, and manometric studies. Her past medical history was significant for cervical cancer. Although brief improvement in symptoms was achieved with botulinum toxin injections and esophageal dilation, she had continued progression of symptoms. This direct involvement of the esophagus by a tumor was not demonstrated by any of the routine preoperative studies.

Results: At the time of surgery, extensive involvement of the diaphragm, esophagus, and pericardium by a tumor was noted. Pathologic analysis of the tumor was consistent with metastatic cervical cancer

Conclusion: Pseudoachalasia has been known to occur in response to both benign and malignant causes. Differentiating between pseudoachalasia and achalasia is often difficult because of the similarities. As in this case, the diagnosis of pseudoachalasia may be made by surgical exploration.

Key Words: Pseudoachalasia, Cancer, Cervical.

INTRODUCTION

Esophageal achalasia is a motor disorder of the esophagus resulting from the degeneration of the cells of the Auerbach's plexus. It is characterized by dysphagia, the absence of peristalsis in the esophageal body, an elevated lower esophageal sphincter pressure, and the absence of relaxation of the lower esophageal sphincter.[1] The majority of patients presenting with these symptoms have idiopathic achalasia, a disorder of unknown etiology that results from degeneration of the esophageal myenteric plexus. Although the cause of this disorder remains elusive, evaluation of patients with Chagas' disease has given some insight into the pathophysiology of achalasia, revealing that as much as 90% of the ganglion cells in the esophagus must be destroyed before symptoms of dysphagia will occur.[2] In rare instances, a collection of symptoms mimicking achalasia may present as a result of extraesophageal causes and is termed pseudoachalasia.

Distinguishing achalasia from pseudoachalasia can be difficult, as the clinical, radiological, and manometric findings are similar.[3] In addition, the low prevalence of pseudoachalasia makes its diagnosis difficult. Torenson[4] reported the incidence of secondary involvement of the esophagus as 3.2 percent in his autopsy series. Various authors have found that 2 to 4% of patients with a manometric diagnosis of achalasia will actually have pseudoachalasia.[3,5-8] Cancer-related causes are by far the most common etiology of pseudoachalasia.[7] However, a benign entity, such as a pancreatic pseudocyst, may also be the cause.[9] Unfortunately, the primary tests used in the diagnosis of achalasia are not entirely reliable for detecting the tumor that causes pseudoachalasia. Barium esophagraphy has a sensitivity of 25% and esophagogastro-duodenoscopy has a sensitivity of 67% for the detection of tumors in patients with pseudoachalasia.[9] Therefore, for pseudoachalasia to be diagnosed in a timely fashion, a high index of suspicion must be maintained.

CASE REPORT

A 37-year-old white female presented with a three-month history of dysphagia that began suddenly with solids and

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progressed to include also liquids. Associated with the dysphagia were retrosternal chest pain, regurgitation of food, and a 30-pound weight loss. During this period of time, she had multiple admissions for dehydration due to her inability to swallow and had diagnostic tests performed, including a chest radiograph, upper GI series, endoscopy, and manometry.

The patient's past medical history was significant for cervical cancer Stage 1B four years prior to this presentation. Pathologic analysis at that time revealed an invasive squamous cell carcinoma with a depth of invasion to one-half the thickness of the cervical wall. The left and right parametrial nodes were positive for metastatic disease; however, the vagina was not involved. The patient underwent a radical hysterectomy and eight cycles of radiation therapy. Annual surveillance, including an evaluation within six months of this presentation, included a PAP smear, chest radiograph, pelvic MRI, and bone scan, which revealed no evidence of recurrent disease.

The patient's physical exam was remarkable for a thin white female in no acute distress. Her abdomen was scaphoid with no organomegally or palpable masses. Her rectal exam was Guaiac negative. No adenopathy was noted. A barium esophagram revealed the classic "bird-beak" deformity, a dilated esophageal body with distal tapering to a smooth stricture at the level of the lower esophageal sphincter **(Figure 1)**. No mucosal irregularities or mass effects were noted. At endoscopy, the body of the esophagus was mildly dilated and particulate matter was present within its lumen. No mucosal irregularities were present **(Figure 2)**. During the initial endoscopic procedures, the endoscope was reportedly passed into the stomach without difficulty. No abnormalities in the stomach or duodenum were noted. Manometry was performed using the station pull-through technique **(Table 1)**. A lower esophageal (LES) pressure of 45 mm Hg was obtained with no relaxation of the LES during swallowing. No effective peristalsis was seen in the body of the esophagus.

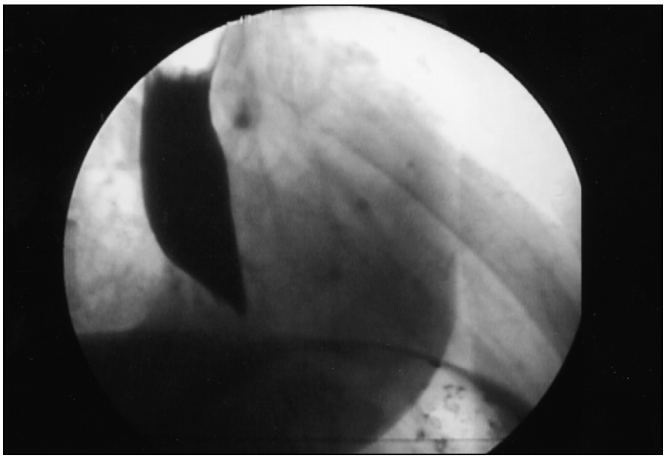

Figure 1. The patient's barium swallow, revealing a mildly dilated esophagus with distal tapering to a smooth stricture at the level of the lower esophageal sphincter.

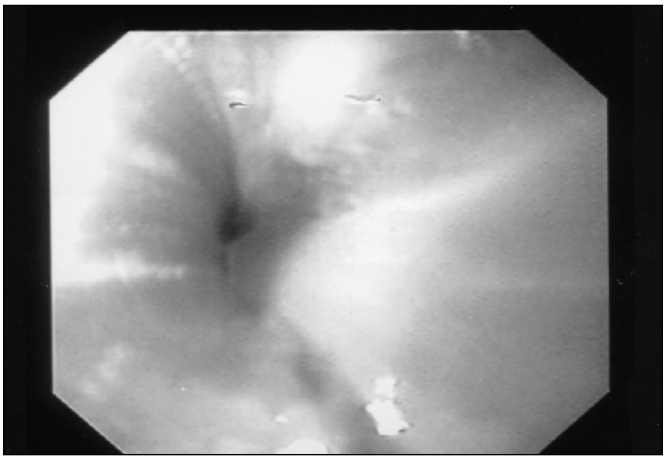

Figure 2. The patient's lower esophageal sphincter, revealing normal mucosa and no evidence of the tumor.

Table 1.
Preoperative Esophageal Manometry

Lower Esophageal Sphincter	
	Resting pressure = 45 mm Hg
	Failure of relaxation with swallowing noted
Esophageal Body	
	Very low amplitude contractions with swallowing
	No effective peristalsis seen in either the proximal or distal esophagus
Upper Esophageal Sphincter	
	Resting pressure = 41 mm Hg
	90% relaxation with swallowing

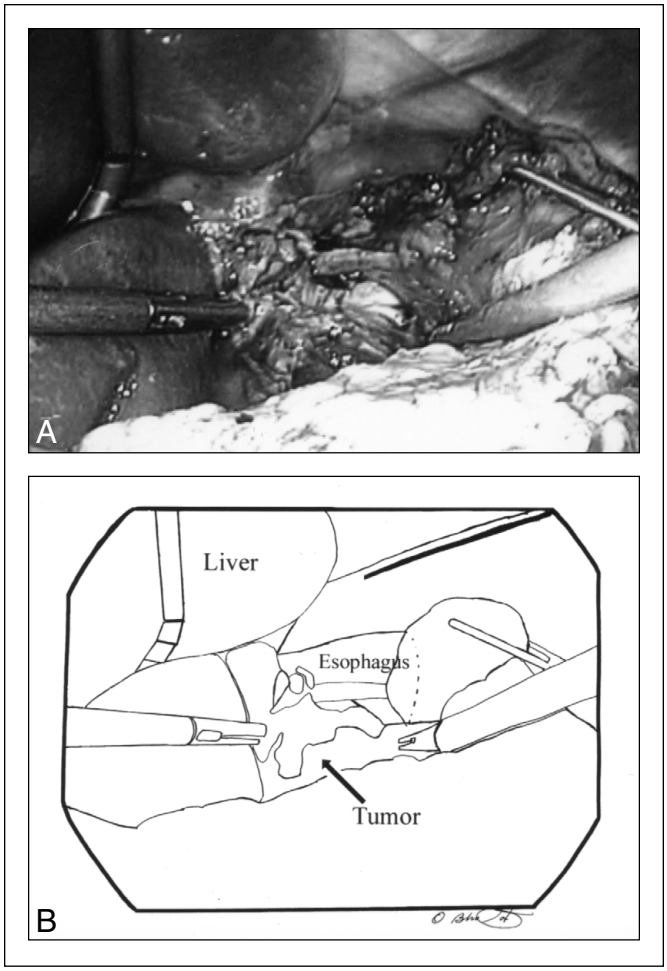

Figure 3. (A) Intraoperative picture showing the tumor invading the esophagus and right crus of the diaphragm. (B) A line drawing representation of the intraoperative findings.

A treatment regimen consisting of injection of the LES with 100 U of botulinum toxin was initiated. The patient described minimal improvement in the symptoms lasting about two weeks. Additionally, the patient was started on oral nifedipine and sublingual nitroglycerin therapy with no improvement. As the patient's symptoms progressed, treatment progressed to esophageal dilation. Endoscopy was repeated and difficulty was reported in passing the endoscope through the gastroesophageal junction. Wire-guided Savary dilation to 54 French was performed under endoscopic guidance. Although initial relief was noted, the patient's symptoms recurred within three days of the endoscopy.

The patient was referred for surgical intervention, and she was considered to be a candidate for a laparoscopic Heller myotomy. At surgery, the right crus of the diaphragm was noted to be calcified, with the esophagus adherent to it. The esophagus was bluntly mobilized off of the right crus, revealing the tumor invading both the esophagus and the diaphragm **(Figure 3)**. The right vagus nerve was encased by the tumor **(Figure 4)** and extension of the tumor into the aorta was suspected. Multiple biopsies of the tumor were taken, and because the frozen section analysis was positive for malignancy, the planned procedure was aborted.

The pathology report was that of a poorly differentiated squamous cell carcinoma **(Figure 5)**. Immunohistochemical stains for cytokeratin (CAM 5.2), chromogranin, and synaptophysin were positive for keratin only. These findings are consistent with metastatic cervical carcinoma. A postoperative CAT scan revealed periaortic adenopathy, invasion of the aorta, and invasion of the pericardium **(Figure 6)**.

DISCUSSION

Pseudoachalasia is a disorder of the esophagus that mimics achalasia. The clinical features that serve to distinguish these two entities are subtle. Although the clinical presentation and diagnostic features are similar, clues are present in both the clinical presentation and diagnostic workup that should be noted. These include an initial

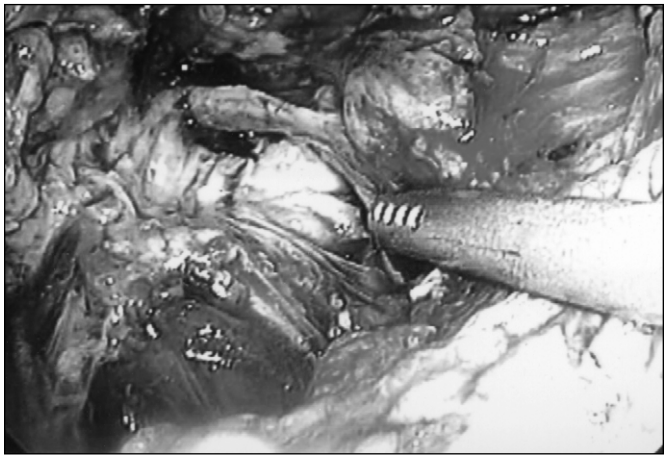

Figure 4. A close up of the patient's esophagus, revealing encasement of the vagus nerve by the tumor.

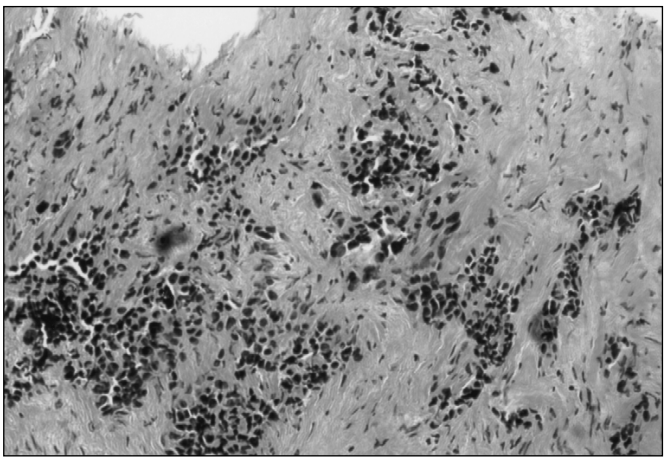

Figure 5. Biopsy of the patient's tumor, revealing a squamous cell carcinoma.

presentation at over 50 years of age, the presence of marked weight loss, a nondilated esophagus, and a duration of dysphagia of less than one year **(Table 2)**.[3,6,7,10] Esophageal compression by an extraluminal mass is the most common cause of pseudoachlasia[10,11] with 71% of the cases resulting from a gastric adenocarcinoma at the GE junction.[7,11,12] The esophageal mucosa usually remains intact, and the mass may have the appearance of a benign intramural lesion.[11,13] Multiple malignant lesions and metastatic tumors have been reported to cause this disorder **(Table 3)**.[7,10,14-17] Therefore, malignancy should always be considered as a potential cause in any patient presenting with achalasia.

Benign entities including truncal vagotomy, sarcoidosis, amylodiosis, chronic idiopathic intestinal pseudoobstruction, familial glucocorticoid deficiency syndrome, juvenile Sjogren's syndrome, aortic aneurysms, and pseudocysts have also been reported as causes of pseudoachlasia.[1,9,18-22]

The pathophysiology of psuedoachalasia is poorly understood. Infiltration of the myenteric plexus has been proposed as a causative factor; however, features of pseudoachalasia without this infiltration have been noted.[23-25] Another theory is that a tumor exerts a paraneoplastic effect, with a resulting vagal neuropathy and eventual degeneration of the myenteric plexus ganglia.[26,27] When present, successful treatment of the tumor may lead to reversal of the esophageal motility

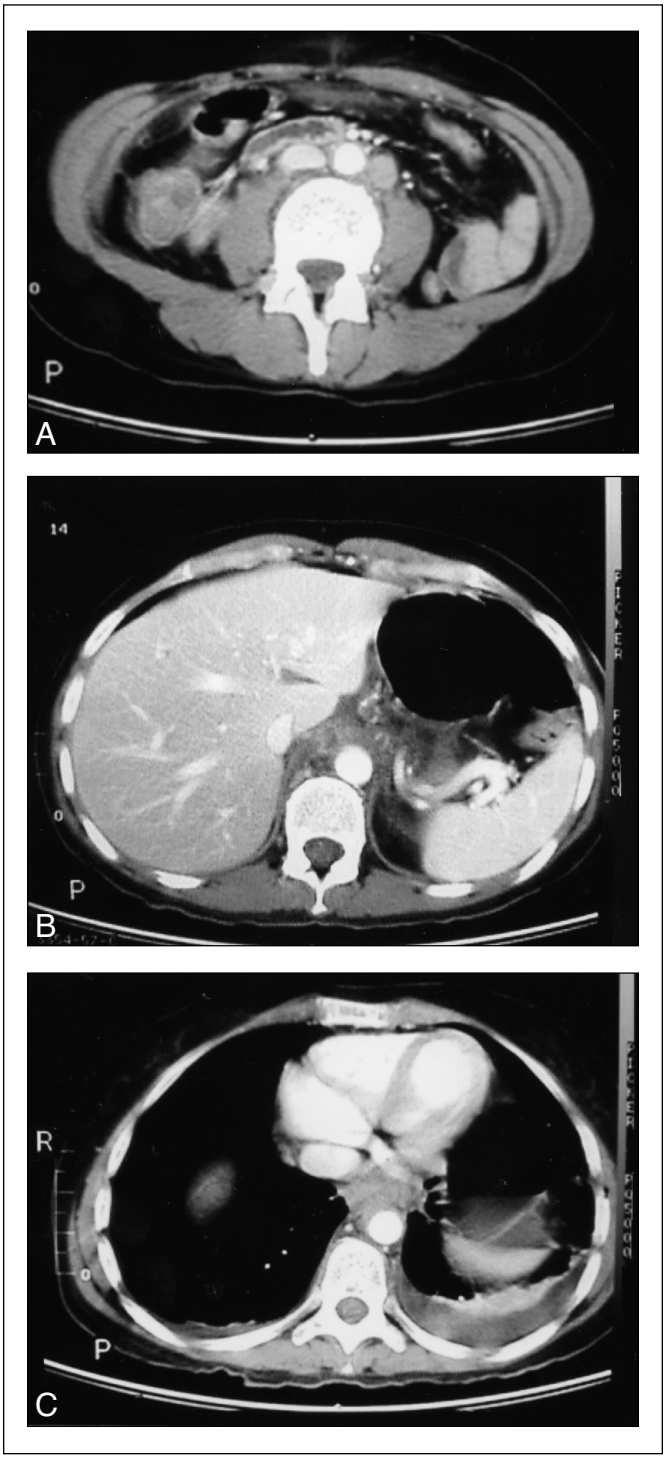

Figure 6. The patient's CT of the abdomen obtained postoperatively revealing (A) periaortic adenopathy, (B) infiltration of the aorta by the tumor, and (C) periaortic mass with invasion of the aorta and pericardium by the tumor.

Table 2.
Clinical Features of Patients with Pseudoachalasia

Onset > 50 yrs
Duration < 1 year
Nondilated esophagus
Marked weight loss

Table 3.
Malignant Lesions That Cause Pseudoachalasia

Gastric adenocarcinoma
Tumors of bronchial origin (adenocarcinoma and oat cell tumors)
Squamous cell carcinoma of the esophagus
Non-Hodgkin's lymphoma
Hodgkin's disease
Pleural mesothelioma
Hepatocellular carcinoma
Prostatic adenocarcinoma
Colonic adenocarcinoma
Pancreatic adenocarcinoma
Renal cell carcinoma
Breast adenocarcinoma
Squamous cell carcinoma of the cervix

abnormality.[26,28] Animal studies have shown that only bilateral cervical vagotomy or dorsal vagal ganglion ablation in the brainstem produces the manometric features of achalasia.[29] These proposed mechanisms involve interruption of the vagal effects on the lower esophageal sphincter and could lead to the findings of pseudoachalasia.

Diagnostic studies, such as an upper GI series, endoscopy, manometry, or CT scans frequently fail to identify an extraesophageal cause for dysphagia.[5,30] However, subtle findings may alert the clinician to the presence of pseudoachalasia. A short segment of the esophagus on the upper GI series or asymmetry of the esophageal narrowing on an upper GI series or CT scan is suggestive of pseudoachalasia. Deformity of the stomach, limited distensibility of the gastric fundus, rigidity of the lower esophagus and mucosal ulceration on endoscopic examination suggests involvement of the esophagus by an extraluminal process **(Table 4)**.[1,30,31]

Table 4.
Diagnostic Features of Patients with Pseudoachalasia

Short segment achalasia on barium swallow
Asymmetry of esophageal narrowing
Asymmetry of esophageal wall thickness
Rigidity of the lower esophagus
Deformity of the stomach
Mucosal ulcerations

If any of these features are present, a diagnosis of pseudoachalasia should be considered. A normal endoscopic biopsy or CT scan does not eliminate pseudoachalasia from the differential diagnosis and a careful workup should be performed, repeating studies if necessary. Endoscopic ultrasound (EUS), an established modality for the imaging and staging of esophageal tumors, is emerging as a method for detecting the underlying occult malignancies of pseudoachalasia.[32] Although invasion of the esophagus can be detected using EUS, it may be difficult to distinguish a tumor from reactive changes to inflammation. Even with these limitations, EUS may detect small, submucosal tumors missed by other diagnostic procedures.[33] Even with careful preoperative testing, surgical exploration may still be necessary to diagnose pseudoachalasia.

CONCLUSION

Pseudoachalasia mimics achalasia and has been known to occur in response to both benign and malignant causes. Distinguishing the two is often difficult because of the rarity of the disorder and the difficulty in detecting the presence of an extraesophageal cause. Specific features of the clinical presentation and diagnostic studies should be sought to make the diagnosis. As in this case, the diagnosis of pseudoachalasia may be made by surgical exploration.

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